Schering-Plough
Research Institute

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November 08, 2000

Dear Dockets Manager:

I am pleased to nominate Dr. Robert C. Johnson, Director of Pathology, Schering-Plough Research Institute in the multidisciplinary working group for drug induced vasculitis. Robert gained his D.V.M. at Auburn University, Auburn, Alabama and a Ph.D. at Cornell University, Ithaca, New York. His thesis project examined organ-specific endothelial cell surface moieties that mediate tumor cell attachment, thereby initiating metastases at the secondary site. This project employed monoclonal antibody development and protein purification. During his postdoctoral studies with Dr. Denisa Wagner at the Center for Blood Research, Harvard Medical School and jointly with Dr. Richard Hynes at Massachusetts Institute of Technology, he was engaged in targeted deletion mouse mutants of endothelial cell surface adhesion molecules, primary P-selection as well E-selection and ICAM-1. Here Robert focused on the role of P-selection in leukocyte rolling and in the attraction of leukocytes to sites of inflammation (wound healing, atheroma formation). His resume is enclosed and lists several publications that are relevant to the topic of endothelial cell biology and therefore vasculopathies.

At Schering-Plough, Dr. Johnson explored the mechanism of a drug induced vasculitis in dogs with one of our new chemical entities in development. Additionally, Dr. Johnson was a member of a task force to test and implement new technologies (gene array, proteomics). In sum, I expect that his expertise in endothelial cell physiology qualifies him to be an exceptional candidate for the working group on drug induced vasculitis.

The nominee is aware of the nomination and is willing to serve on the working group if selected.

Thank you for your consideration in this matter.

Sincerely,

Mark Cartwright,
Senior Director of Pathology

00N-0930

Nom 27

ROBERT CRAIG JOHNSON

Office: (973) 940-4352

EMPLOYMENT:

1/95 – present	Director, Pathology - Schering-Plough Research Institute, Lafayette, NJ Responsible for toxicologic pathology portion of safety evaluation studies including protocol development, scientific review and monitoring contracted studies. Represent Drug Safety for Project Development Teams; compile preclinical sections of Briefing Documents, Investigator's Brochure and regulatory submissions (IND, IDD). Collaborative support to Discovery groups. Member of New Technologies Task Force. Implemented multi-user, LAN based digital image acquisition and archiving system.
6/93 – 7/94	Pathologist - Division of Comparative Medicine, USDA Center for Human Nutrition and Aging, Boston, MA (part-time)
1986 – 1991	Laboratory Instructor - Cornell University, College of Veterinary Medicine, Ithaca, NY Teaching Experience: General Pathology and Systemic Pathology
1986 – 1988	Pathology Resident Instructor - Cornell University, College of Veterinary Medicine, Ithaca, NY Senior Veterinary Student Rotation in Pathology
1986 – 1988	Instructor - Cornell University, College of Veterinary Medicine, Ithaca, NY Student Seminar Series
10/83 – 6/85	Lab Assistant - Department of Pathology/Parasitology, College of Veterinary Medicine, Auburn University, Auburn, AL
6/84 – 9/84	Lab Assistant - Mycology Lab, Centers for Disease Control, Atlanta, GA

EDUCATION:

1992 – 1995	Postdoctoral Fellow, The Center for Blood Research, Harvard Medical School, Boston, MA
1992 – 1995	Research Affiliate, Massachusetts Institute of Technology, Center for Cancer Research, Cambridge, MA
1988 – 1992	Ph.D. in Biochemistry, Cancer Cell Biology Laboratories, Cornell University, Ithaca, NY
1986 – 1988	Residency Training, Comparative Pathology, Cornell University, College of Veterinary Medicine, Ithaca, NY
1982 – 1986	D.V.M. with Honors, Auburn University, Auburn, AL
1979 – 1983	B.S. with High Honors, Auburn University, Auburn, AL

PROFESSIONAL ORGANIZATIONS:

- Diplomate: American College of Veterinary Pathologists
- American Association for the Advancement of Science
- Graduate Student Council, Cornell University
- Society of Toxicologic Pathologists
- United States and Canadian Academy of Pathology, Inc.
- Society of Toxicology

AWARDS/HONORS:

- NIH, National Research Service Award
- Graduate Research Assistantship - Cornell University
- First Place, Research Poster Day - Cornell University
- Phi Kappa Phi
- Doctor of Veterinary Medicine with Honors
- Bachelor of Science with High Honors
- Dean's Honor Roll - Auburn University
- Maxine McDaniel Memorial Scholarship Award - Auburn University

CONTINUING EDUCATION:

1999	International Conference and Workshops on Molecular Morphology, Santa Fe, NM
1998	International Business Conference (IBC), Molecular Toxicology, Washington, DC
1996	Pharmaceutical Education and Research Institute, Inc. (PERI), Basic Training Course on Pharmacology, Somerset, NJ
1995	International Life Sciences Institute, Histopathology Seminar on Respiratory System of Laboratory Animals, Atlanta GA
1995	Cornell University, College of Veterinary Medicine, Eastern North American Diagnostic Veterinary Pathology Conference, Cobleskill, NY
1995	Cell Vision, Modern Methods in Analytical Morphology, Atlantic City, NJ
1995	Pharmaceutical Toxicology Training Course, Pharmaceutical Education and Research Institute PERI Washington, DC
1990	Pathology of Laboratory Animals, Armed Forces Institute of Pathology, Bethesda, MD
1990	Concepts of Molecular Biology, American Association of Pathologists, Bethesda, MD

PUBLICATIONS:

Leach MW, Frank DW, Berardi MR, Evans EW, Johnson RC, Schuessler DG, Radwanski E, Cartwright ME. Renal changes associated with naproxen sodium administration in cynomolgus monkeys. Toxicol. Pathol. 27:295-306, 1999.

Grace MJ, Xie L, Musco ML, Cui S, Gumani M, DiGiacomo R, Chang A, Indelicato S, Syed J, Johnson R, and Nielsen L. The use of laser scanning cytomtery to assess depth of penetration of adenovirus p53 gene therapy in human xenograft biopsies. American Journal of Pathology 155: 1869-1878, 1999.

Johnson RC, Dovey-Hartman BJ, Syed J, Leach MW, Frank DW, Sinha DP, Mirro EJ, Little JM, and Halliwell WH. Vacuolation in renal tubular epithelium of Cd-1 mice: An incidental finding. Toxicol. Pathol. 26:789-792, 1998.

PUBLICATIONS (CONTINUED):

Nielsen LL, Gurnai M, Syed J, Dell J, Hartman B, Cartwright ME and Johnson RC. Recombinant E1-deleted adenovirus-mediated gene therapy for cancer: efficacy studies with p53 tumor suppressor gene and liver histology in tumor xenograft models. Human Gene Therapy 9:681-694, 1998.

Johnson RC, Chapman SM, Dong ZM, Ordovas JM, Mayadas TN, Herz J, Hynes RO, Schaefer EJ and Wagner DD. Absence of P-Selectin delays fatty streak formation in mice. J. Clin. Invest. 99:1037-1043, 1997.

Subramaniam M, Frenette PS, Saffaripour S, Johnson RC, Hynes RO and Wagner DD. Defects in hemostasis in P-Selectin-deficient mice. Blood 87:1238-1242, 1996.

Pinsky DJ, Naka Y, Liao H, Oz MC, Wagner DD, Mayadas TN, Johnson RC, Hynes RO, Lawson CA and Stern DM: Hypoxia-induced exocytosis of endothelial cell Weibel-Palade bodies: A mechanism for rapid neutrophil recruitment following cardiac preservation. J. Clin. Invest. 97:493-500, 1996.

Frennette PS, Johnson RC, Hynes RO and Wagner DD: Platelets roll on stimulated endothelium *in vivo*: An interaction mediated by endothelial P-selectin. PNAS 92:7450-7454, 1995.

Johnson RC, Mayadas TN, Frenette PS, Lacasce AS, Subramaniam M, Mebius R, Hynes RO, and Wagner DD: Blood cell dynamics in P-selectin deficient mice. Blood 86:1106-1114, 1995.

Augustin HG, Kozian DH and Johnson RC: Differentiation of endothelial cells: Analysis of the constitutive and activated cell phenotypes. Bioassays 16:901-906, 1994.

Mayadas TN, Johnson RC, Rayburn H, Hynes RO and Wagner DD: Leukocyte rolling and extravasation are severely compromised in P-selectin-deficient mice. Cell 74:541-554, 1993.

Johnson RC, Zhu D, Augustin-Voss HG and Pauli BU: Lung endothelial dipeptidyl peptidase IV is an adhesion molecule for lung metastatic rat breast and prostatic carcinoma cells. J. Cell Biol. 121:1423-1432, 1993.

Pauli BU, Johnson RC, Widom J and Cheng C-F: Endothelial cell adhesion molecules and their role in organ preference of metastasis. Trends in Glycoscience and Glycotechnology 15:405-414, 1992.

Pauli BU, Johnson RC and El-Sabban M: Organotypic endothelial cell surface molecules mediate organ preference of metastasis. In: Endothelial Cell Dysfunction, Simionescu N, Simionescu M (eds.), Plenum Press, New York 1992.

PUBLICATIONS (CONTINUED):

Johnson RC: Canine spirocercosis and associated esophageal sarcoma. The Compendium 14:577-580, 1992.

Johnson RC, Augustin-Voss HG, Zhu D and Pauli BU: Endothelial membrane vesicles in the study of organ preference of metastasis. Cancer Research, 51:394-399, 1991.

August-Voss HG, Johnson RC and Pauli BU: Modulation of endothelial cell surface glycoconjugate expression by organ-derived biomatrices. Exp. Cell Res. 192:346-351, 1991.

Pauli BU, Augustin-Voss HG, El-Sabban M, Johnson RC and Hammer DA: Organ preference of metastasis: The role of endothelial cell adhesion molecules. Cancer Metastasis Reviews, 9:175-189, 1990.

ORAL PRESENTATIONS:

Spermatogenesis: Places User's Group Meeting. Parsippany, NJ, 1998 (invited speaker).

P-Selectin and Inflammation: New Jersey Society of Histotechnology. Kenilworth, NJ, 1996 (invited speaker).

The Role of P-Selection in Fatty Streak Formation: Minisymposia. ACVP, 1996.

Blood Cell Dynamics in P-Selection-Deficient Mice. Minisymposia. ACVP, 1995.

Lung endothelial membrane vesicles in the study of organ preference of metastasis. Minisymposia. FASEB J (75):842, 1991.

Preferential binding of lung metastatic tumor cells to lung-derived endothelial cell surface vesicles. Minisymposia FASEB J (4):A1134, 1990.

ABSTRACTS:

Talmadge JE, Hirai M, Kelsey L, Shabram P, Hutchins B, Johnson R, LaFace D, Wen SF, Warkentin PL, Mills K, Vaillancourt M and Maneval DC. Nod-scid studies examining adenovirus-p53 purging of tumor cells from hematopoietic stem cell products.

Grace M, Xie L, Johnson RC, Cui J, Syed J, Musco ML, Gurnani M, Shi B and Nielsen LL. Solid tumor penetration of SCH58500 (p53 adenovirus) after intraperitoneal dosing as assessed by immunohistochemistry and laser scanning cytometry. Keystone Symposium on Molecular and Cellular Biology of Gene Therapy (Salt Lake City, UT), January 14-20, 1999.

ABSTRACTS (CONTINUED):

Grace M, Nuovo G, Johnson RC, Cui J, Syed J, Musco ML, Xie L, Gurnani M, Greenberg R, Schaefer E and Nielsen LL. Solid tumor penetration of SCH58500 (p53 adenovirus) after intraperitoneal dosing as assessed by immunohistochemistry, p53 RT-PCR in SITU, and laser scanning cytometry. American Society of Gene Therapy, 1998.

Johnson RC, Schmahai TJ, Pennline KJ, Statkevich P and Rosenblum IY. Chronic toxicity study of recombinant human interleukin-10 (rhuIL-10) in cynomolgus monkeys, Society of Toxicology, 1998.

Leach MW, Frank DW, Johnson RC, Berardi MR, Evans EW, Radwanski E, Schuessler DG and Cartwright ME. Pharmacokinetics and renal changes associated with subacute naproxen sodium administration in cynomolgus monkeys. Presented at the 48th Annual Meeting of the American College of Veterinary Pathologists, Albuquerque, New Mexico, November 18-21, 1997. Vet Pathol 34:481.

Syed J, Gurnani M, Dell J, Hartman B, Cartwright ME, Nielsen L, Johnson RC. Evaluation of recombinant E-1 deleted adenovirus-mediated liver Pathology and p53 tumor suppressor gene efficacy against tumor metastasis in mice. Presented at NSH Convention/Symposium, Columbus, OH, Oct. 1997.

Hartman BJ, Johnson RC, Leach MW, Frank DW, Sinha DE, Mirro EJ, Little JM and Halliwell WH. Vacuolation in renal tubular epithelium of mice: An incidental lesion. Microscopy & Microanalysis '97. August 10-14, 1997.

Leach MW, Frank DW, Johnson RC, Berardi MR, Evans EW and Cartwright ME. Renal lesions associated with subacute administration of naproxen sodium in cynomolgus monkeys. Poster presented at the Sixteenth International Symposium of the Society of Toxicologic Pathologists, Beaver Creek, Colorado, June 22-26, 1997, Proceedings p 9.

Berardi MR, Johnson RC, Leach MW and Rosenblum IY (sponsor). Toxicity of Naproxen Sodium Administered Orally to Cynomologus Monkeys for Two Weeks. Society of Toxicology, 1997.

Leach MW, Snyder EA and Johnson RC. Two-Dose Intravenous Toxicity Study of SCH 55700. A Humanized Anti-IL-5 Monoclonal Antibody in Cynomologus Monkeys. Society of Toxicology, 1997.

SCH 351125 DISCUSSION POINTS

- **SCH 351125 interaction with the cynomolgus monkey receptor**
  Ki approximately 100-300nM

- **Toxicologic implications of inhibition – immunomodulatory?**
  32-base pair deletion, human CCR5 allele (confers resistance)

- **Structural/metabolism concerns**

- **Reproductive toxicology issues**
  Embryo-fetal development study in monkeys (vs rabbits)

- **Polytherapy regimen**
  Combination toxicity study (compatible with HAART Tx)
  Drug interactions

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